DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

- OCT 30 2002

Warning Letter

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

via Federal Express

Raed Aqel, M.D.
Department of Cardiology
Birmingham Veterans Affairs Medical Center
700 South 19th Street
Birmingham, Alabama 35233

Dear Dr. Aqel:

The purpose of this Warning Letter is to inform you of the objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at your clinical site and to request a prompt reply. Ms. Patricia Smith of the FDA New Orleans District conducted the inspection on June 24-28, 2002.

The purpose of the inspection was to determine if your activities as a clinical investigator in the [redacted] sponsored by [redacted] complied with applicable FDA regulations. The [redacted] is a device as that term is defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 321(h)].

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemption (IDE), Premarket Approval Application (PMA), and Premarket Notification [510(k)] submissions are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

Our review of the inspection report prepared by the New Orleans District Office reveals violations of requirements of Title 21, Code of Federal Regulations (21 CFR), Part 812 – Investigational Device Exemptions and Part 50 – Protection of Human Subjects. Ms. Smith listed her findings on a Form FDA-483, "Inspectional Observations," and discussed these findings with you.

The violations noted on the FDA-483 and resulting from our subsequent review of the inspection report are summarized below:

1. **Failure to conduct the study in accordance with the investigational plan, the investigator's agreement, and conditions of approval imposed by the IRB [21 CFR 812.110(b)].**

The IRB requires you to submit an annual progress report for its continuing review of the ongoing research. You failed to submit an annual report to the IRB by March 31, 2002, the expiration date of the study approval. You continued the research after the expiration of IRB approval and after the IRB notified you that it suspended its approval of the study on April 8, 2002.

You failed to enroll subjects according to the inclusion/exclusion criteria. For example, you enrolled subject [redacted] who had an [redacted] within [redacted] hours of the study procedure and subject [redacted] who had a [redacted] greater than [redacted] even though according to the protocol their conditions would exclude them from the study. In addition, there are many subject case histories containing unexplained changes in the [redacted]. For example, the records of subjects [redacted] and [redacted] originally documented [redacted] values of [redacted] and [redacted], respectively, but the values were later (without written explanation) changed to [redacted] the minimum inclusion value.

You failed to perform all required tests at study visits. Your records contained numerous instances where study procedures, including laboratory testing, were either not performed or were not consistently followed at scheduled examinations. For example, subjects [redacted] and [redacted] did not have tests performed. Cardiac medication was not prescribed according to the investigational plan. For example, subjects [redacted] and [redacted] were not administered [redacted] as scheduled.

2. Failure to obtain informed consent (21 CFR Part 50 and 21 CFR 812.100).

You failed to ensure that a legally effective informed consent was obtained from each study subject. In addition, the informed consents do not contain a contact person for questions regarding their rights as human subjects in the study. It was also noted that the informed consents used and signed by [redacted] subjects at your site contain language not easily understandable to those subjects. Medical terminologies are not clearly defined in lay-language. For example: lumen, atherectomy, modalities, and stenting to scaffold the lesion, are not defined in the consent document.

The violations listed above are not intended to be an all-inclusive list of deficiencies at your site. As a clinical investigator, it is your responsibility to ensure that the investigation you participate in is conducted in accordance with applicable FDA regulations.

Please advise this office, in writing, within 15 working days of receipt of this letter, of the specific steps that you have taken to correct these violations or other violations known to you, and to prevent the recurrence of similar violations in current or future studies. In addition, please provide a list of your current investigational studies and include the name

of the study sponsor and the date of IRB approval. The failure to respond may result in further regulatory action without notice.

A copy of this letter has been sent to the Food and Drug Administration, New Orleans District Office, 6600 Plaza Drive, Suite 400, New Orleans, Louisiana 70127. We request that a copy of your response be sent to New Orleans District Office and to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 2098 Gaither Road, Rockville, Maryland 20850, Attention: Kevin M. Hopson, Consumer Safety Officer.

Sincerely yours,

Charma Akonor, RN, RAC

for Philip J. Frappaolo
Acting Director
Office of Compliance
Center for Devices and Radiological Health

cc: [redacted]